DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

APR 18 2005

PreAnalytix GmbH
c/o Ms. Jing Zhang
Regulatory Affair Manager
Becton, Dickinson and Company
BD Diagnostics, Preanalytical Systems
1 Becton Drive, MC 300
Franklin Lakes, New Jersey 07417

Re: K042613
Evaluation of Automatic Class III Designation
PAXgene™ Blood RNA System
Regulation Number: 21 CFR 866.4070
Classification: Class II
Product Code: NTW

Dear Ms. Zhang:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your petition for classification of the PAXgene™ Blood RNA System that is intended for the collection, storage, and transport of blood and stabilization of intracellular RNA in a closed tube and subsequent isolation and purification of intracellular RNA from whole blood for RT-PCR used in molecular diagnostic testing.

FDA concludes that this device, and substantially equivalent devices of this generic type, should be classified into class II. This order, therefore, classifies the PAXgene™ Blood RNA System, and substantially equivalent devices of this generic type into class II under the generic name, RNA Preanalytical Systems. This order also identifies the special controls applicable to this device.

FDA identifies this generic type of device as:

21 CFR 866.4070 RNA Preanalytical Systems. RNA Preanalytical Systems are devices intended to collect, store, and transport patient specimens and stabilize intracellular RNA from the specimens for subsequent isolation and purification of the intracellular RNA for RT-PCR used in in **vitro** molecular diagnostic testing.

In accordance with section 513(f)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360c(f)(1)) (the act), devices that were not in commercial distribution prior to May 28, 1976 (the date of enactment of the Medical Device Amendments of 1976 (the amendments)), generally referred to as postamendments devices, are classified automatically by statute into class III without any FDA

rulemaking process. These devices remain in class III and require premarket approval, unless and until the device is classified or reclassified into class I or II, or FDA issues an order finding the device to be substantially equivalent, in accordance with section 513(i) of the act (21 U.S.C. 360c(i)), to a predicate device that does not require premarket approval. The agency determines whether new devices are substantially equivalent to previously marketed devices by means of premarket notification procedures in section 510(k) of the act (21 U.S.C. 360(k)) and Part 807 of the FDA regulations (21 CFR 807).

Section 513(f)(2) of the act provides that any person who submits a premarket notification under section 510(k) for a device may, within 30 days after receiving an order classifying the device in class III under section 513(f)(1), request FDA to classify the device under the criteria set forth in section 513(a)(1). FDA shall, within 60 days of receiving such a request classify the device. This classification shall be the initial classification of the device type. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the **Federal Register** classifying the device type.

On February 28,2005, FDA filed your petition requesting classification of the PAXgene™ Blood RNA System into class II. The petition was submitted under section 513(f)(2) of the act. In accordance with section 513(f)(1) of the act, FDA issued an order on February 18,2005, automatically classifying the PAXgene™ Blood RNA System in class III, because it was not within a type of device which was introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, which was subsequently reclassified into class I or class II. In order to classify the PAX gene™ Blood RNA System into class I or II, it is necessary that the proposed class have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use.

After review of the information submitted in the petition, FDA has determined that the PAXgene™ Blood RNA System, intended for the collection, storage, and transport of blood and stabilization of intracellular RNA in a closed tube and subsequent isolation and purification of intracellular RNA from the whole blood for RT-PCR used in molecular diagnostic testing can be classified in class II with the establishment of special controls. FDA believes that class II special controls provide reasonable assurance of the safety and effectiveness of the device.

Failure of the system during collection, RNA stabilization and/or purification could yield an RNA sample of low quality and quantity. Low quality RNA, when tested, could result in a falsely low or high RNA transcript signal level that could lead to inaccurate diagnosis and/or improper patient management. Low quantity of RNA could render the samples unusable for downstream RT-PCR applications. Specimens would need to be recollected, causing possible delay in diagnosis. In addition, depending on specimen type, recollection could pose additional patient risk (e.g., tissue biopsy). The degree of risk varies depending on the disease or condition/stage being diagnosed or managed. Therefore. use of results to adjust a treatment regimen, without considerations of other clinical factors, poses risks. The measures FDA recommends to mitigate these risks are described in the guidance document, "Class II Special Controls Guidance Document: RNA Preanalytical Systems

(RNA Collection, Stabilization and Purification Systems for RT-PCR used in Molecular Diagnostic Testing)", which includes recommendations for performance validation and labeling.

In addition to the general controls of the act, RNA Preanalytical Systems are subject to the following special controls: "Class II Special Controls Guidance Document: RNA Preanalytical Systems (RNA Collection, Stabilization and Purification Systems for RT-PCR used in Molecular Diagnostic Testing)". Section 510(m) of the act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the act, if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device. FDA has determined premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device and, therefore, the device is not exempt from the premarket notification requirements. Thus, persons who intend to market this device must submit to FDA a premarket notification submission containing information on the RNA preanalytical system they intend to market prior to marketing the device.

A notice announcing this classification order will be published in the **Federal Register.** A copy of this order and supporting documentation are on file in the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852 and are available for inspection between 9 a.m. and 4 p.m., Monday through Friday.

As a result of this order, you may immediately market this device, subject to the general control provisions of the act and the special controls identified in this order.

If you have any questions concerning this classification order, please contact Uwe Scherf at (240) 276-0496.

Sincerely yours,

for Steven I. Gutman, M.D., M.B.A.
Director
Office of In *Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

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PreAnalytix GmbH
c/o Ms. Jing Zhang
Regulatory Affair Manager
Becton, Dickinson and Company
BD Diagnostics, Preanalytical Systems
1 Becton Drive, MC 300
Franklin Lakes, New Jersey 07417

Re: k042613
Trade/Device Name: PAXgene™ Blood RNA System
Regulatory Class: III
Product Code: NTW
Dated: February 18,2005
Received: February 18,2005

Dear Ms. Zhang:

This letter corrects our not substantially equivalent (NSE) letter of February 18,2005 regarding the PAXgene™ Blood RNA System in which the letter was incorrectly addressed to the submission correspondent, BD Diagnostics, instead of to the applicant, PreAnalytiX GmbH.

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above. We have determined the device is not substantially equivalent to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments or to devices that have been reclassified into class I (General Controls) or class II (Special Controls). This decision is based on the fact that we are not aware of a legally marketed preamendments device labeled or promoted for the collection, storage, and transport of marketed preamendments device labeled or promoted for the collection, storage, and transport of blood and stabilization of intracellular RNA with subsequent isolation and purification of the intracellular RNA from whole blood for RT-PCR used in molecular diagnostic testing.

Therefore, this device is classified by statute into class III (Premarket Approval), under Section 513(f) of the Federal Food, Drug, and Cosmetic Act (Act). Section 515(a)(2) of the Act requires a class III device to have an approved premarket approval application (PMA) before it can be legally marketed, unless the device is reclassified.

Any commercial distribution of this device prior to approval of a PMA, Product Development Protocol (PDP), or the effective date of any order by the Food and Drug Administration re-classifying this device into class I or II, would be a violation of the Act. Clinical investigations of this device must be conducted in accordance with the investigational device exemptions (IDE) regulations.

The Food and Drug Administration Modernization Act of 1997 (FDAMA), in section 207, deals with the Evaluation of Automatic Class III Designation. Under this section a manufacturer, whose device is found to be not substantially equivalent to a predicate device, can request FDA to make a risk-based classification for their device. However, I believe that based on the review of your device, general controls would be inadequate and special controls difficult to develop, to provide reasonable assurance of the device's safety and effectiveness. However, you have the right to make such a request of this agency. For additional information on your options under Section 207, please refer to our guidance entitled, "New Section 513(f)(2) - Evaluation of Automatic Class III Designation, Guidance for Industry and Staff." This document is available on the World Wide Web/CDRH Home Page at: http://www.fda.gov/cdrh/modact/classiii.html.

If you wish to pursue the marketing of this device and need information or assistance for preparing investigational or premarket submissions, please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll free number (800) 638-2041 or (301) 443-6597, or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

for Steven I. Gutman, M.D., MBA
Director
Office of In Vitro Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure